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14. ABSTRACT

For the U.S. Military, war-related traumatic injury deaths exceeded 5,000 in the last decade, and many more soldiers and marines have been seriously injured by improvised explosive devices, high-velocity munitions, and vehicular events. These events have brought the problem of the acute coagulopathy of trauma to the fore. The goal of this project was to increase basic knowledge about the coagulopathy specifically associated with severe trauma. Our objectives were to assemble a precise and detailed database on coagulation factor levels over the course of resuscitation of severely injured, hemorrhaging, patients. Our proposed research was to be conducted with a 24 hour delay of informed consent, which was approved by our IRB. The Air Force ultimately denied approval for a delayed consent. The results are thus limited. Nevertheless, we enrolled 15 patients including several who were shot, others who were severely injured in other ways and four who ultimately died. Despite the small number of patients recruited, the demographics and methods of injury were typical of modern American civilian urban Level I trauma center populations. Furthermore, all but one had types and degrees of injury and clinical presentations that suggested a risk for coagulopathy; eleven of

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REVIEW ARTICLE

Transfusion practice in military trauma

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SUMMARY. Modern warfare causes severe injuries, and despite rapid transportation to theater regional trauma centers, casualties frequently arrive coagulopathic and in shock. Conventional resuscitation beginning with crystalloid fluids to treat shock causes further dilutional coagulopathy and increased hemorrhagic loss of platelets and coagulation factors. Established coagulopathy was difficult to reverse in the face of uncontrolled hemorrhage. Because many of the casualties met conventional plasma and platelet transfusion criteria on admission, thawed AB plasma was prepositioned in the trauma receiving area and used in a 1:1 ratio with red cells for resuscitation and fresh whole blood was used as a source of platelets. Retrospective assessments of this 1:1 therapy strongly suggested that it resulted in improved hemostasis, shorter ventilator times, and improved survival. Component therapy, when available, appears to be as effective as fresh whole blood. In field emergencies, fresh whole blood can be lifesaving.

Key words: battlefield blood support, expedient transfusion, military medicine, war surgery.

> 'He, who would be a surgeon, must take up his tools and follow the army'. Hippocrates

In the current conflicts in Iraq and Afghanistan, soldiers with severe injuries caused by high-velocity weapons and explosive devices presented in large numbers to military hospitals. As a result, military physicians are seeing patients who require massive transfusion at four to five times the frequency seen in civilian practice.

This concentrated surgical experience with massive transfusion has re-emphasizing some old truths. Specifically, resuscitation with crystalloid fluids and plasma-poor red cell concentrates leads rapidly to dilutional coagulopathy (Counts *et al.*, 1979; Mannucci *et al.*, 1982; Murray *et al.*, 1995). Hypothermia and acidosis are also increasingly frequent with increasingly severe injury and caused profound coagulopathy by themselves (Kashuk *et al.*, 1982; Jurkovich *et al.*, 1987; Ferrara *et al.*, 1990). Finally, there is a renewed recognition of a syndrome of acute coagulopathy of trauma (Simmons *et al.*, 1969; Faringer *et al.*, 1993; Brohi *et al.*, 2003; MacLeod *et al.*, 2003). All these findings suggest that there is a need for the early use of plasma in the resuscitation of those most likely to progress to massive transfusion in order to actively prevent dilutional coagulopathy and treat the acute coagulopathy of trauma (Ketchum *et al.*, 2006; Malone *et al.*, 2006).

Now, a retrospective study of this recent military experience and an unpublished review of patients from 16 civilian trauma centres modelled on the military study show that there is a 50% reduction in mortality to be associated with the increased use of plasma early in resuscitation of massively transfused trauma patients (Borgman *et al.*, 2007). These reports have created a demand for rapid access to thawed plasma, often in the form of prepositioned units of thawed AB plasma in trauma receiving units and, in turn, for blood centres to be able to supply large amounts of this uncommon component (Hess *et al.*, 2006; Holcomb *et al.*, 2007). In this review, the authors describe the evolution of our understanding of the coagulopathy of trauma and its treatment.

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INJURY, TRAUMA SYSTEMS AND TRAUMA SURGERY

Injury

Injury is the leading cause of death for individuals aged 1–45 years in the developed world and is rapidly becoming the second leading cause of death worldwide (WHO, 2002; Mathers *et al.*, 2005). Injuries affect people of all ages but have their most profound social consequences in the loss of young adults from the working population. Injury is the most common cause of the loss of years of productive life, with rates four times that of cancer and heart disease.

Every year, about 1·2 million people in the United States are hospitalized for injury (Nathens *et al.*, 2004). They will typically receive about 1 unit of blood apiece during an initial admission (Como *et al.*, 2004). Thus, injured patients use about 8% of the red cell supply, about 1·2 million units each year.

Civilian trauma systems

To deal with this epidemic of injury, trauma care has regionalized across the United States and Canada in specialized trauma centres at the centre of casualty transport networks. Transport, as in the military, is by helicopter or highly organized ground units. These centres function to standards developed by the Committee on Trauma of the American College of Surgeons, and the largest two dozen serve as centres for training and research. Their standards for care and transfusion have evolved from expert opinion and published research and are largely contained in the Advanced Trauma Life Support course and accreditation guidelines published by the American College of Surgeons (MacKenzie *et al.*, 2006). The guidelines require a massive transfusion protocol to be accredited as a trauma centre but do not specify what it must say.

The largest of these centres, called Level 1 Trauma Centers, see more than 1200 patients a year or 250 who have an injury severity score of >15 and must have a trauma surgeon, anaesthesiologist, orthopaedic surgeon, thoracic surgeon and neurosurgeon readily available at all times, as well as full blood bank support. The authors' centres are the Shock Trauma Center at the University of Maryland, Baltimore, among the largest such centres in the world, with over 5600 admissions annually, and the Brooke Army Medical Center in San Antonio, Texas, which provides care to 1500 trauma patients annually, about 1/4 of all trauma in the seventh biggest city in the United States.

Regionalization of trauma care is found on a military model of rapid casualty evacuation that relies heavily on prehospital care by technicians trained to basic or advanced emergency medical technician or occasionally paramedic levels. Once in the trauma unit, casualties are rapidly evaluated by physical assessment, biophysical instrumentation and laboratory tests and by rapid imaging such as focused abdominal sonography for trauma and 13-s whole-body open frame X-ray scans. Emergent surgery can be started in minutes if necessary and carried through staged procedures in multiple body cavities supported by periods of intervening intensive care. The quality of such care is measured as injury-specific morbidity and mortality.

Como *et al.* (2004) reviewed the use of blood at the Maryland Shock Trauma Center. In 2000, 5649 patients were brought to the centre directly from the scene of injury and 480 received red cells during their admission. Even among this group, most received only a few units, whereas a few receive large numbers, so that the most common number of units given was 2, the median transfused patient received 6 units and the average number of units transfused to a patient receiving red cells was 11. Only 146 patients received more than 10 units during their admission, and only 68 received more than 20 units. As only 61% of the red cells were given on the first day in the hospital, the number of acute massive transfusions, individuals receiving 10 or more units of red blood cell (RBC) in the first 24 h, was 90 in that year, of the order of 1·7% of all admissions.

This experience with acute massive transfusion of 90 patients a year was shared among 10 faculty trauma surgeons. Individual experience with massive transfusion was necessarily limited and only accumulated over many years. Because of this paucity of experience, massive transfusion protocols were based on expert opinion and negotiated between trauma specialists and blood bank medical directors. In practice, this meant that un-cross-matched group 'O' red cells were available in the trauma centre, but plasma was issued only after a blood type was available. The system appeared to work well, with injury-specific mortality rates below national averages and wastage rates of blood products of less than 0·5%.

Military trauma systems

Basic military trauma care begins with self-care and buddy care, and every soldier now carries haemostatic bandages and tourniquets with them into combat. Medics support small units with gauze and haemostatic bandages, intravenous fluids, pain control, splinting, primary casualty evacuation, and battalion aid stations provide primary casualty collection, airway stabilization, fracture stabilization and some emergency non-cavitary surgical procedures. At the same time, ground and air ambulance units go as far forward as they can to pick up casualties. Such evacuation is generally to large combat support hospitals.

Military transfusion practice, at least for those countries trying to provide state-of-the-art care for their citizen soldiers, attempts to mirror the practice of their best civilian trauma centres. However, it is difficult to maintain fully tested platelets in remote and primitive locations, and the choices involved in supporting this aspect of field medical care had not been resolved at the time the war started.

In support of the war, the US military blood programme processes blood collected on military bases into tested components and ships these components by air to the Middle East via a staging area in Qatar. The combat support hospitals receive regular shipments of red cells, with a minimum age of 32 days on arrival in country, and fresh frozen plasma and cryoprecipitate. Platelets, now collected by apheresis in country, did not become routinely available until early in 2006. Therefore, in 4·5 years of sustained operations, about 6000 units of fresh whole blood were given to about 1000 casualties out of 86 000 total units of red cells and whole blood administered to about 5000 casualties.

Trauma surgery and trauma surgery training

Since the Vietnam War, the field of trauma surgery has developed as an academic specialty. There are now 1084 trauma centres and 2500 active diplomates of the American Board of Surgical Critical Care in the United States (Branas *et al.*, 2005). The formal training of a trauma surgeon involves a 5-year general surgical residency, frequently with a built-in sixth or seventh year for research, and is followed by a year or two of specialty trauma and surgical critical care training.

The rising quality of trauma research has been recognized in US National Institutes of Health funding of the PULSE initiative and Resuscitation Outcome Consortium (Carrico *et al.*, 2002). The investment of resources in research has meant the ability to maintain and explore large data registries and follow groups of similarly injured patients to understand causes of death and suggest better methods of treatment. The first randomized clinical trials in trauma patients had demonstrated the utility of a bolus of hypertonic saline, that presurgical massive resuscitation with crystalloid fluids is not necessary and is probably harmful (Vassar *et al.*, 1993; Bickell *et al.*, 1994; Dutton *et al.*, 2002)

HAEMORRHAGE, COAGULOPATHY AND HAEMORRHAGE CONTROL

With good modern care, profound neurological injury and haemorrhage are the two most common causes of death following trauma (Shackford *et al.*, 1989; Sauaia *et al.*, 1995). Haemorrhage is the most frequent cause of potentially preventable deaths in the hospital. Potentially preventable hemorrhagic deaths occur when patients arrive at trauma centres with potentially surgically correctable injuries but bleed to death before anatomic control of bleeding is achieved or is effective. By definition, such patients need better circulatory support to keep them alive and better haemorrhage control to stop their bleeding.

The distinction between anatomic correction of injury and surgical control of haemorrhage is critical because it serves as the functional definition of coagulopathy. Surgeons develop a sense of how closely tissue must be approximated to stop normal bleeding. Continued oozing at intravenous catheter or suture sites, at sites of reasonable tissue approximation, and on expanses of denuded tissue that exceeds the surgeons' expectations is deemed coagulopathic bleeding.

Coagulopathic bleeding broadly correlates with the concentrations and functional activities of plasma coagulation and anticoagulant proteins and platelets (Counts *et al.*, 1979). These concentrations and activities can be affected by a variety of pathophysiological processes occurring in the setting of acute trauma, including blood loss, dilution, acidosis, hypothermia, tissue injury leading to factor consumption and fibrinolysis (Armand & Hess, 2003)

Loss of part of the blood volume and dilution of the coagulation mechanism occur with all significant bleeding. The body has only small amounts of the structural elements of blood clots, about 10 g of fibrinogen and 10 mL of platelets (1·25 trillion platelets), circulating in the blood under normal conditions. Significant shock in previously healthy young individuals usually represents the loss of 30–40% of the blood volume or more. It generally takes the body a day to produce that much fibrinogen and several days to replace that number of platelets. Acute replacement of the lost volume, either by physiological vascular refill or with administration of crystalloid or non-plasma colloid solutions, results in an equivalent degree of dilution. By the time the platelet count falls below 100×10^9 per litre, the skin bleeding time increases, and when plasma concentration of the individual coagulation factors fall below 25–40% of normal levels, both clinical coagulopathy and increases in the prothrombin time and partial thromboplastin times occur (Counts *et al.*, 1979). A low haematocrit will also prolong the bleeding time (Valeri *et al.*, 2001).

Despite the randomized clinical trial showing that the administration of crystalloid solutions increased the mortality in presurgical patients with penetrating truncal injury and a second showing that maintaining injured patients in a mildly hypotensive state during evaluation in the trauma centre did not increase mortality, preventing dilution has been hard to achieve. It is customary to start several intravenous lines in the injured for the potential administration of fluid, blood and drugs, and just to have them in case of need. Once there, they must be kept open. Fluid boluses are given to clear lines after blood samples are drawn to drive administered drugs into the central circulation and to ensure that lines are open while blood products are being started. For years, surgeons were taught to give litre boluses of crystalloid fluids to test for volume depletion. Without great attention to fluid discipline, the amounts of crystalloid fluid administered can mount rapidly and administration of multiple litres is not unusual.

Dilution can also occur because of the composition of modern blood components Armand & Hess (2003). Products made from whole blood loose red cells and platelets in leucocyte reduction filters and are diluted by anticoagulants and additive solutions. When these products are recombined in a beaker in a ratio of 1 unit of red cells to 1 unit of plasma to 1 unit of platelets (1 : 1 : 1), the resulting hematocrit is 29% the platelet concentration about 88×10^9 per litre and the plasma concentration about 65%. However, with conventionally stored products, only 90% of the red cells and 70% of the platelets circulate after re-infusion, and with platelets stored in non-plasma additive solutions, the final plasma concentrations will be even lower. Thus, during massive transfusion with only blood components given in the optimal 1 : 1 : 1 ratio, the blood concentrations for each of the components lead to an anaemic, thrombocytopenic and coagulopathic state near the transfusion triggers for each of the components, and administration of any one component in excess only results in dilution of the other two. Adding any crystalloid only exacerbates this problem.

Hypothermia is common in the injured because they cannot move to keep warm and are at risk for conductive, radiative and evaporative heat loss. Tissue hypoxia reduces mitochondrial activity, further reducing heat production. Heat loss can be made worse in the emergency room by exposure for examination and treatment and in the operating room with the exposure of large areas to evaporative cooling. With a fully open abdomen, evaporative cooling can result in the loss of 1 °C every 40 min Hirshberg *et al.*, 1999). Hypothermia has a direct effect on the rates of the enzymatic rates of the coagulation proteins, reducing those rates by half at 30 °C. Hypothermia also decreases the synthesis of fibrinogen (Martini, 2007). However, the greatest effect of hypothermia is on the activation of platelets through the interaction of von Willebrand's factor with the platelet-activating receptor complex, GPIb–IX. Kermode *et al.* (1999) have shown that below 30 °C, this reaction fails to activate platelets from the majority of individuals, and Jurkovich *et al.* (1987) have shown that injured patients with a core temperature less than 32 °C and significant bleeding rarely survive. At higher temperatures, a combination of reduced platelet activation and slowed coagulation factor enzyme kinetics has more modest effects on clotting.

Acidosis also affects clotting, destabilizing the coagulation protein complexes that normally form on the surfaces of activated platelets and profoundly reducing their activity. Thus, half of the normal activity of the Xa–Va complex is lost at a pH of 7·2, 70% is gone at pH 7 and 80% gone at pH 6·8 (Meng *et al.*, 2003). Acidosis also increases metabolic degradation of fibrinogen (Martini & Holcomb 2007). In pre- and postsurgical trauma patients, the most important single factor associated with coagulopathy was acidosis (Cosgriff *et al.*, 1997; Brohi *et al.*, 2007).

Extensive injury causes consumption of coagulation factors and platelets, so that in polytrauma patients, factors and platelets lost or consumed at one site of injury are not available for use at another. Injury also activates anticoagulant mechanisms, and acidosis and low vascular shear increase the expression of thrombomodulin, protein C and tissue factor pathway inhibitor. All these pathways work by consuming procoagulant factors.

Clots that do form in severely injured patients are less stable than that in healthier individuals. Lower fibrinogen concentrations result in less dense fibrin clots (Fries *et al.*, 2006). The reduced local thrombin concentrations achieved in the activation of dilute plasma result in thinner strands of fibrin being laid down and less thrombin-activated fibrinolysis inhibitor being activated (Blomback, 2001). Tissue plasminogen activator released in response to low flow is not inhibited normally because plasminogen activator inhibitor is suppressed by acidosis. Injured patients are thus susceptible to inappropriate fibrinolysis.

The end result of all these pressures on the clotting mechanism is that blood clots slowly and poorly in injured patients. The resulting weak clots are more likely to be disturbed in the manipulation necessary for patient care, and the clots are likely to break down prematurely. Experienced surgeons understand these principles and use an array of approaches to control haemorrhage in the face of coagulopathic bleeding. These approaches include local control of bleeding with tissue sealants such fibrin glues and fibrin dressings, regional approaches such as abdominal packing in 'damage control' procedures and systemic approaches such as rewarming and the administration of procoagulants and antifibrinolytics. These techniques appear to save lives in situations where patients commonly died in the past, but they have not been rigorously tested.

THE ACUTE COAGULOPATHY OF TRAUMA

In 2003, Brohi and his colleagues and MacLeod and her colleagues both published large series of trauma patients who presented to the trauma centre already coagulopathic before significant haemodilution had taken place (Brohi *et al.*, 2003; MacLeod *et al.*, 2003). Although this early coagulopathy of trauma had been recognized in Vietnam casualties and later, its frequency and serious implications for survival had not been widely appreciated (Simmons *et al.*, 1969; Faringer *et al.*, 1993). Coagulopathy had been described as secondary to hypothermia and acidosis, thus the decade-long focus is on reversing these two physiological derangements (Cosgriff *et al.,* 1997). Brohi and his colleagues described a group of 2000 injured patients arriving by helicopter at the Royal London Hospital and showed that the incidence of prolonged plasma coagulation times was proportional to injury severity but that in patients with equivalent injury severity scores, those with coagulopathy had higher mortality. MacLeod and her colleagues from Miami described 23 000 patients admitted to the Ryder Trauma Center over a 7-year period and showed that those who presented with an elevated prothrombin time had a markedly increased mortality. As would be expected, this excess mortality was evident from the first few hours when most deaths from uncontrolled haemorrhage occur. The effect of these two papers arriving at the time of the second Iraq invasion was to increase the sense of urgency about the need to control coagulopathy in the seriously injured.

THE EXPERIENCE IN THE SECOND IRAQ WAR

As noted above, in the early phases of the war, casualties were few and tended to be treated with local stabilization and evacuation to large treatment facilities in Kuwait. With the capture of Baghdad and the collapse of the Iraqi national army, the situation changed. The US military occupied a large area of central Baghdad, the 'Green Zone' including the Ibn Sina Hospital, which was taken over and used as a central receiving hospital for the increasing numbers of high-velocity weapons and improvised explosive device casualties caused by the evolving civil, sectarian and anti-American violence. Other combat support hospitals were distributed across the country. As the violence grew, increasing numbers and proportions of severely injured casualties presented, and it was soon recognized that in the combat support hospitals, up to 30% of the transfused casualties were presenting with the acute coagulopathy of trauma and 8% were requiring massive transfusion.

Initially, conventional care patterns of resuscitation were established, including resuscitation with crystalloid fluids and group O red cells, followed by attempted correction of the coagulopathy with thawed plasma and fresh whole blood as a source of platelets after a blood type was available. However, it was recognized that allowing patients to become even more coagulopathic early in the course of resuscitation while a blood type was obtained and plasma thawed was not optimal, and in discussions between the authors, a system of having prethawed group 'AB' plasma already available in the casualty receiving area was established. At the same time, group O fresh whole blood collected but not used for one casualty was held warm for up to 24 h and was occasionally available for immediate use in subsequent casualties (Hughes *et al.*, 2007). With experience, the surgeons learned to recognize injury patterns and physiological measures that predicted massive transfusion and to start resuscitation with a 1 : 1 ratio of plasma to red cells (Schreiber *et al.*, 2007).

The surgeons observed that the new system appeared to work better in two ways. First, despite the high levels of injury severity, the incidence of coagulopathic bleeding appeared to go down during the first hour of resuscitation when plasma or fresh whole blood was used as the resuscitation fluid. This resulted in a surgical field where diffuse oozing was absent, allowing easier control of surgical bleeding. Also, by not using crystalloid fluids for resuscitation, the incidence of pulmonary oedema and abdominal compartment syndromes seemed to decrease, allowing patients to spend less time on ventilators and with open abdomens from damage control procedures and decompression laparotomies. To confirm these clinical observations, a study of massively transfused patients was undertaken.

THE BORGMAN STUDY

The resulting study, now published in the *Journal of Trauma* by Borgman and his colleagues, is a retrospective analysis of 246 patients who received at least 10 units of red cells, fresh whole blood or a combination of both products in the first 24 h of care between November 2003 and September 2005 (Borgman *et al.*, 2007). The series was gathered from the Joint Theater Trauma Registry created to gather information on all casualties treated in theatre and represents 4·6% of all the casualties treated in the time period. The striking finding of the study was that despite equivalent injury severity scores, the patients who received less than 1 unit of plasma for every 4 units of red cells had a 65% mortality, whereas those who received at least 1 unit of plasma for every 2 units of red cells had a mortality of 19%. The remaining patients who received an intermediate amount of plasma, 1–2 units for every 4 units of red cells, had a mortality of 34%. Patients who received the low ratio of plasma to red cells typically died of uncontrolled haemorrhage, 92% of all deaths, after a mean of 2 h of care. Among patients who received the highest ratios of plasma to red cells, deaths occurred at a mean of 38 h, with only 37% of deaths resulting from uncontrolled haemorrhage (but with relatively more from sepsis and multiple organ failure) and ultimately used fewer units of red cells. The results suggest that giving more plasma early allows surgical control of haemorrhage, saving lives and perhaps even red cell units. The observed reduction in mortality is very large, so that the number needed to be treated to save one life is only 2.

There are many problems with this kind of retrospective review and many ways that selection bias can influence the results. These patients may have presented with patterns of injury that led to more urgent and RBC intensive resuscitations. Their deaths may have occurred at times when plasma and other resources for care were not available. As more resources and better care became available in theatre, mortality may have decreased for reasons unrelated to the administration of plasma.

Nevertheless, the data are plausible. Severely injured patients who receive 10 units of red cells and, on average, 1 unit of plasma are almost assured to be severely coagulopathic. As they continued to bleed and received an average of 21 units of RBC and less than 3 units of plasma before they died, they would have be expected to became even more coagulopathic, contributing to death from uncontrolled haemorrhage.

A second finding of the study, not mentioned in the published report, is of particular interest to transfusion medicine physicians. This finding is that when the data were reanalysed to see if there was an independent effect of fresh whole blood, there was none. As long as equivalent amounts of plasma were given, the fresh whole blood was not better than stored red cells, and all the stored red cells used in theatre were at least 32 days after collection.

THE PERKINS STUDY

A second study, as yet unpublished, has been presented by Major Jeremy Perkins. It examined the effect of platelets, given either as fresh whole blood or apheresis platelets collected in theatre, and compared 149 patients who did not receive any components containing platelets with 285 who did in the course of massive transfusion. Larger numbers of patients resulted from a later study over a longer time (2004–2006).

In this retrospective review, patients who received any platelets had a 20% lower mortality that was evident by 5 h and persisted to 30 days. Again, patients who received their platelets as fresh whole blood or apheresis platelets in conjunction with 32-day or older red cell concentrates had equivalent mortality.

The utility of this simple 'time to death' comparison of two subsets of a massively transfused population is again weakened by confounding. Many of the patients in this study were also reported in the Borgman study. Many who received platelets also received plasma either as fresh whole blood, plasma in platelets or thawed plasma in conjunction with platelets from a better prepared blood system.

THE CIVILIAN TRAUMA CENTRE STUDY

Because the data from these studies were so striking, and almost impossible to repeat or review in the war environment, surgeons at 26 civilian trauma centres were asked to submit data on patients massively transfused in their centres in the previous year. Results from 466 patients in 16 centres were received, and again a correlation was observed, with patients receiving relatively more plasma and platelets having a higher survival rate. Furthermore, the variability in survival between these 16 large trauma centres ranged from 25 to 70% and the ratio of plasma : RBC from 1 : 5 up to 1 : 1. These unpublished results are undergoing further review but have been presented widely and have attracted a $10 million direct congressional appropriation to conduct a prospective study.

WHAT IS THE STANDARD OF CARE?

On the basis of the Borgman study, the US Army Surgeon General has issued a clinical practice guideline suggesting resuscitation of severely injured soldiers with equal numbers of units of red cells and plasma where possible. Several civilian centres in the United States have placed thawed AB plasma in blood refrigerators in their emergency departments and are collecting data. As additional institutions attempt to do this, the supplies of AB plasma are becoming scarce. The attempt to limit transfusion-related acute lung injury by removing plasma donated by women exacerbates this scarcity. It should be remembered that only massively transfused patients have been suggested to benefit by this treatment and that they represent only a small fraction (1–2%) of all civilian trauma patients. It should also be remembered that conventional transfusion guidelines recommend plasma transfusion to bleeding multitrauma patients when their International Normalization Ratio (INR) exceeds 1·5. Such patients can be identified by simple clinical algorithms based on vital signs and injury patterns that identify patients likely to require massive transfusion and to have a prolonged INR on admission with almost 80% sensitivity (McLaughlin *et al.*, 2008).

Widely available point of care devices can measure an INR in minutes, and clinical prediction algorithms can identify severely injured patients with a high probability of an abnormal INR in seconds. The usual delay associated with waiting for a laboratory-measured INR and blood type followed by thawing plasma can be shortened with clinical prediction of acute coagulopathy and pre-thawed plasma in the blood bank or trauma center.

Whether there is a significant clinical difference between giving a 1 : 1 ratio of plasma to red cells or some lower ratio such a 1 : 2 will probably require several large clinical studies to resolve. In the mean time, trying to make products available and working collaboratively with trauma surgeons to understand the benefits and the risks of a high plasma to red cell transfusion ratio in the massively injured seems the most appropriate course.

CONFLICTS OF INTEREST

The opinions expressed in this work are those of the authors and are not to be construed as those of the US Army or the US Department of Defense. This is a US Government work, and there is no copyright.

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